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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,302	03/07/2001	Patrick F. Kelly	2427/1G685US1	2679

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EXAMINER
QIAN, CELINE X

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/07/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,302	KELLY ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-30* is/are pending in the application.

4a) Of the above claim(s) *19-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 2-37 are pending in the application. Claims 19-37 are withdrawn from consideration for being directed to non elected subject matter. Claims 2-18 are currently under examination.

This Office Action is in response to the Amendment filed on 2/13/03. The Amendment has been entered.

Response to Amendment

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

The rejection of claims 2-16 under 35 U.S.C.112 2nd paragraph has been withdrawn in light of Applicants' clarification of the claims.

The rejection of claims 2-18 under 35 U.S.C.103 (a) is moot in view of the new grounds of rejection necessitated by Applicants' amendment of the claims.

Response to Arguments

Election/Restrictions

Applicants requested rejoin of Groups II-V, claims 19-30 with Group I. Applicants traverse the finality of the restriction. The invention of Groups II-V are patentably distinct for reasons set forth of the record mailed on 12/6/01, and the decision is made final as indicated in the Office Action mailed on 2/23/02. Claims 19-30 are withdrawn from further consideration by the examiner in accordance with 37 CFR 1.142(b) for being directed to non elected subject matter. (See MPEP § 809.02(c) and § 821.01 through § 821.03). If Applicants traverse the

finality of the restriction requirement, Applicant may file a petition under 37 CFR 1.144 for review of the restriction requirement. The finality of the restriction requirement is maintained at present. Accordingly, claims 19-30 are withdrawn from consideration for being directed to non-elected subject matter. Claims 2-18 are currently under examination.

Applicant's arguments with respect to the rejection of claims 2-18 under 35 U.S.C. 103(a) have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection Necessitated By Applicants' Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hennemann et al (1999 Experimental Hematology, Vol 27, pages 817-825), in view of Onodera et al., Porter et al., Unchida et al. and Rebel et al.

Hennemann et al. teach a method of transduction of a retroviral vector comprising GFP in human umbilical cord blood stem cells capable of multi-lineage engraftment in SCID mice. Hennemann et al. teach that CD34+CD38- subpopulation of the cord blood cells are purified and pre-stimulated with cytokines such as IL-3, IL-6 and SCF. Hennemann et al. also teach that the producer cell medium containing viral particles passes through a 0.45-um filter before transduction of the stem cell. Hennemann et al. further teach that the plate is pre-coated with

fibronectin CH-296. However, Hennemann et al. does not teach that the retroviral vector is a RD114 pseudotyped vector.

The teachings of Onodera et al., Porter et al., Unchida et al., and Rebel et al. was discussed in the previous office action mailed on 8/14/02.

It would have obvious to one of ordinary skilled in the art to combine the teaching of Hennemann et al., Onodera et al. and Porter et al. to develop a method of transducing hematopoietic stem cells with retroviral particle pseudotyped with RD114. Hennemann et al teach a method of transducing a retroviral vector comprising GFP in human umbilical cord blood stem cells, wherein the stem cells repopulate the lineage and express GFP upon engraftment into the SCID mice. Onodera et al. and Porter et al. both teach that retroviral vectors pseudotyped with RD114 produces high titer and transduces cells efficiently. Although Onodera et al. does not provide an example of transduce hematopoietic stem cells, the article teaches that since MPSV-based retroviral vectors provide expression immature progenitor cells, they may be effective for gene therapy trials using hematopoietic stem cells. Porter et al. demonstrate that efficient transduction can be done in CD34+ bone marrow cells using RD114 pseudotyped vectors. Although Porter et al. teach that the transduction is accomplished by co-cultivation, it is not the only way to transduce these cells. Hennemann et al. teach that the transduction step can be accomplished by contacting cells and virus on plates pre-treated with fibronectin, wherein the producer cells and supernatant are substantially removed. Onodera et al. teach that efficient transduction using retroviral particles packaged with RD114 can be achieved with producer cell free viral particles. Therefore, it would have been obvious to one of ordinary skill in the art to transduce hematopoietic stem cells using retroviral particles pseudotyped with RD114 (either co-

culture or substantially free of producer cells or supernatant). The ordinary artisan would have been motivated to do so since both articles teach effective transduction by such method, and the advantage of RD114 resistant to human complement. The level of skill of art is high. Absent evidence to the contrary, one of ordinary skill of art would have reasonable expectation or success to practice the claimed method and achieve high transduction efficiency using the RD114 pseudotyped retroviral vector. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would have obvious to one of ordinary skilled in the art to combine the teaching of Hennemann et al., Onodera et al. and Porter et al. and Uchida et al. to develop a method of transducing hematopoietic stem cells with lentiviral vector pseudotyped with RD114. The ordinary skill of art would have been motivated to do so because Uchida et al. teach that using lentiviral vector in transducing hematopoietic cells isolated from mobilized peripheral blood is efficient and improves transduction efficiency of hematopoietic stem cells over MLV vector. The level of skill of art is high. Absent evidence to the contrary, one of ordinary skill of art would have reasonable expectation or success to practice the claimed method and achieve high transduction efficiency using the RD114 pseudotyped lentiviral vector. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

The obviousness to develop a method of transducing stem cells by using RD114 pseudotyped retroviral vector is discussed above. Removing producer cells and producer cell supernatant by ultracentrifugation is a routine method to concentrate retroviral particles as demonstrated by Rebel et al. Therefore, it would have been obvious to one of ordinary skill of

art to practice the method of transducing stem cells with RD114 pseudotyped retroviral vectors that are substantially free of producer cell and producer cell supernatant, wherein the producer cells are removed by ultracentrifugation. The ordinary artisan would have been motivated to do so because said method would concentrate the viral particle and increase titer as taught by Rebel et al. The ordinary artisan would have reasonable expectation of success because such method is provided in Rebel et al. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
April 29, 2003

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER